REMARKS

Applicants thank the Examiner for conducting a telephonic interview on February 2, 2006, with Applicants' representative, Yu Lu, regarding the Final Office Action. Applicants also thank the Examiner for withdrawing the objection to the specification, and the rejections under 35 U.S.C. §§ 101, and 112, second paragraph.

The Claims

Claims 1, 3-5, and 8-11 are pending in this application.

Applicants have amended Claims 1, 3, 10, and 11 to clarify the subject matter claimed. Support for these amendments and claims can be found throughout the specification. *See, e.g.*, paragraph **[0019]** of the published specification **(U.S. 2004-00255343 A1)** supports the Claim 3 amendment "via homologous recombination." The title, abstract, and paragraphs **[0001]** and **[0006]** support the amendment to Claims 1, 3, 10, and 11.

Rejection under 35 U.S.C. § 112, first paragraph

(1) Written Description

The Examiner maintained the written description rejection to Claims 1, 8, and 9, but withdrew the written description rejection to Claims 3-5 in view of Applicants' amendments.

The Examiner states that the term "defective" encompasses "any gain or loss of function," and thus "the present claim encompasses a genus of mice that completely lack Caspase-9 expression, to mice that vastly over express endogenous Caspase-9." The Examiner argues that the disclosed QACXG Caspase-9 mutation "is substantially different from and does not adequately describe a mouse that is defective because of an increase in Caspase-9 expression or because of a gain-of-function mutation in the Caspase-9 gene" (emphasis added).

Not acquiescing in the reasoning of the Office Action, and solely for the purpose of advancing prosecution, Applicants have amended Claims 1, 3, and 10, and their dependent claims. Applicants submit that the Claim 1 amendment now requires the defective Caspase-9

gene to cause a "deficiency" in Caspase-9 function. The term "deficient" refers to various loss-of-function Caspase-9 mutations (see, for example, the Merriam-Webster online dictionary, which defines "deficient" as "an amount that is *lacking or inadequate*"). Thus the scope of the amended claims effectively excludes the defectiveness due to an *increase* in Caspase-9 expression, or due to any other *gain-of-function* mutations in the Caspase-9 gene. As amended, the claims only encompass complete and partial loss-of-function mutations.

As the Examiner acknowledges, it was common knowledge at the time of filing that there were numerous known ways to create loss-of-function mutations in a target gene (*e.g.*, the Caspase-9 gene). In addition, other methods well-known in the art to affect gene expression are specifically referred to in the specification. See, *e.g.*, page 5, lines 25-31 of the specification. Pursuant to MPEP 2163 (Sec. IIA(2)):

"Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)" (emphasis added).

Applicants submit that there was no need to describe additional loss-of-function mutations in detail in the specification, in view of the disclosure in the specification, and the knowledge in the art. Applicants have thus provided adequate written description for a representative number of species of mice deficient in Caspase-9 function due to a defective Caspase-9 gene.

The Examiner also rejects Claim 3, because the integration step allegedly does not require homologous recombination.

Applicants have amended Claim 3 to specifically recite "via homologous recombination" to clarify the subject matter claimed, thereby obviating the rejection.

For all of the above reasons, and in view of Applicants' claim amendments, Applicants respectively request that the Examiner reconsider and withdraw the § 112, first paragraph, written description rejection.

(2) Enablement

Claims 1, 3-5, and 8-11 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to enable a skilled artisan to practice the invention commensurate in scope with the claims. Applicants traverse.

The Office Action does not explain why these claims are not enabled to their full scope. During the February 2, 2006 interview, the Examiner argued, concerning the enablement rejection, that the specification has not enabled a skilled artisan to make all gain-of-function Caspase-9 mutations.

Because of the claim amendments and arguments presented above, Applicants submit that the amended claims are enabled to their full scope because gain-of-function mutations are no longer within the scope of the claimed invention.

For substantially the same reason, Applicants note that Claim 10 should have been allowed even without the amendment introduced in this response. The defective Caspase-9 in Claim 10 is explicitly described as being non-functional because it lacks the critical QACXG motif. In view of the examples in the specification, Claim 10 already satisfies the written description and enablement requirements.

In view of the above arguments and claim amendments, Applicants respectively request that the Examiner reconsider and withdraw the enablement rejection under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the foregoing amendments and arguments, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this submission, please charge the fees, or credit any overpayment of the same, to our **Deposit Account No. 18-1945**, under the charge number **VPI/98-104 CIP CON**.

Dated: Monday, February 6, 2006

Respectfully submitted,

By_____

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